

AN ADDRESS ON A CHARACTERISTIC ORGANISM OF CANCER.

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[From the Pathological Laboratory of the Royal Infirmary.]

[FOR DESCRIPTION OF FIGS. 1 AND 2 SEE COLOURED LITHOGRAPH.]

FOR some years past I have been occupied, so far as my routine duties and other researches would allow me, in tracing the mode of growth of cancer in different organs. By this study I hoped to map out the steps of the process, and, by learning the manner of its growth, perhaps to obtain an insight into the factors determining the departure of the tissues from their normal behaviour and arrangements. In the course of these studies I met with appearances which I could not fit into modes of cell growth and nuclear proliferation, and one of these cases so puzzled me that I asked my principal pathological assistant, Mr. W. F. Robertson, to experiment on it with every possible combination of stains, with a view to the possible differentiation of some of these structures. His attempts were soon successful, for by a process of double staining, first with fuchsine and then with iodine green, without passing the sections through any specially decolorising agent, the iodine green replaced the fuchsine in everything, with the exception of certain bodies.

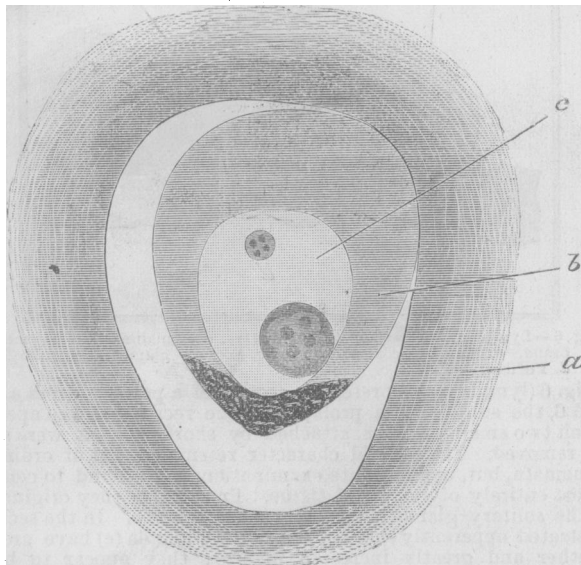


Fig. 3.—Large epithelial cell *b*; in space surrounded by fibrous tissue *a*, and showing at lower part nucleus; *c*, vacuole containing two organisms.

Directions for Staining.—1. Saturated solution of fuchsine in 2 per cent. carbolic acid in water. 2. One per cent. solution of iodine green (Grüber's), in 2 per cent. carbolic acid in water. Place section in water. Then stain in fuchsine ten minutes or longer. Wash for a few minutes in water. Then wash for *half a minute* in absolute alcohol. From this put the section into the solution of iodine green, and allow it to remain well spread out for *five minutes*. From this, rapidly dehydrate in absolute alcohol, pass through oil of cloves, and mount in balsam.

The fact that I had observed special structures in a case of cancer I mentioned at the Medico-Chirurgical Society of Edinburgh on June 4th, 1890, but I said that I did not know whether they were special nuclei or a foreign organism.

This of course led to further investigation, and to the examination of other cases of cancer, with the result that the structure was found in all those examined. For laboratory use it was necessary to have a convenient name for these, so I called them fuchsine bodies, and this name I propose to adhere to until their relations to cancer and their biological status is determined.

With this discovery all kinds of possible error were suggested to my mind: Were they accidental impurities in my material, bottles, or stains? Was it a mere piece of staining legerdemain? Were they the nuclei of tissue cells in exaggerated formative and reproductive activity? Or were they simple globes of some form of degeneration? All these questions I set myself to answer. Tissues from the same bottles, preserved in the same fluid and cut at the same time, were examined without any indication whatever of accidental contamination. The idea of staining legerdemain was excluded by the impossibility of producing the effect in non-cancerous parts. Although from their perfect roundness and homogeneous hyaline-like structure it seemed impossible they should be nuclei, still the remote possibility had to be dealt with. Organising inflammation of serous membranes showed that the nuclei of the formative cells did not give the reaction; neither did the cells in tubercle of the lungs, in typhoid lesion of the intestine, in inflammatory affections of the meninges, lungs, etc., in granulations, nor in the organs of an embryo at the fourth month. Then as to degenerations: fatty degenerations and infiltrations, waxy degeneration in different organs, colloid goitre, myxoma, myxomatous sarcoma, degenerative changes of epithelium as in tubular nephritis, spinal cord degenerations, and, in fact, all kinds of morbid material which I could think of, were examined, and, with the exceptions I shall refer to presently, with a like negative result. Then as regards their presence in other

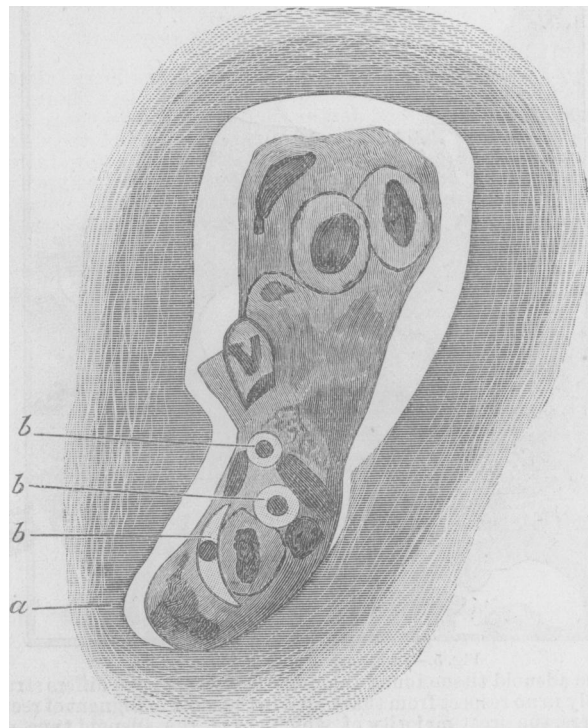


Fig. 4.—Mass of epithelium lying in alveolus^w wall (*a*) formed of fibrous tissue; *b b b*, encapsuled organism.

tumours, the sarcomata were examined early, and gave negative results, although in one case in which there were extremely large cells, and which I thought might be an unusually large-celled sarcoma, the bodies were found, and their presence I think probably indicates that the original view I was inclined to take of this growth was wrong. In simple tumours, such as fibromata, papillomata, myomata, etc., they were not found. In venereal warts and condylomata they were not found, nor in primary syphilitic sores, nor in the ulcerated tissue and crust of a syphilitic skin affection. A tumour taken out of my practical class material and labelled

"adenoma of mamma," and which is very rich in adenomatous structures, showed the bodies. A tumour of the dura mater from the same material, which has been in my possession for the last seven years, and which I think is certainly a gumma, showed the lymphatics in its neighbourhood to contain numbers of these fuchsine bodies; of this case, as well as the preceding, I at present know nothing. Recently I had a syphilitic case in the *post-mortem* room which was both exceptional and extraordinary—

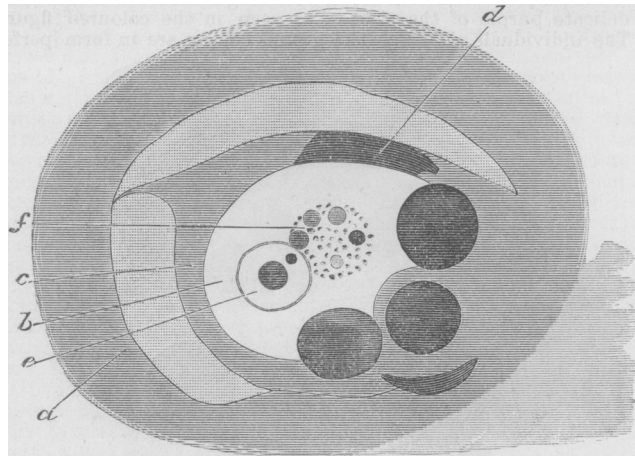


Fig. 5.—Wall of alveolus *a*; *b*, large vacuole surrounded by remains of epithelial protoplasm showing at *d* nucleus; *e*, encapsuled organism lying in vacuole; *f*, degenerating organism showing spores in its interior.

case in which, some six or seven weeks after primary infection, there was not only a skin eruption, but extensive destructive lesion of the fauces and larynx, and even of the bones of the vertebrae behind the fauces. This case had absolutely defied treatment. In the larynx of this case I found a few fuchsine bodies. One other tumour I may mention—an aural polypus sent over for report from the Throat and Ear Department. I found this polypus to be in its greater part fibromyxomatous in structure,

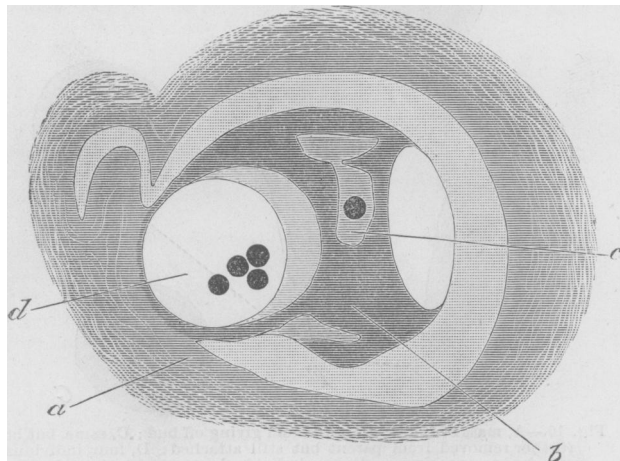


Fig. 6.—Fibrous wall, *a*, containing mass of epithelium, *b*; *c*, nucleus with parasite in interior; *d*, vacuole with four fungi.

but in its deeper part adenomatous, and in this adenomatous part I found a few fuchsine bodies. I wrote to Dr. McBride asking him if he had any suspicion of its being malignant, and he replied that he did not know, but that it was no sooner removed than it commenced to grow again, and that he could not get the patient to come regularly to have it attended to. In three cases of gelatinous degeneration of the knee-joint examined they were found in one, and this case had, I believe, old sinuses. In a subject in the *post-mortem* room, with a large ulcer on the leg with a large island of skin in the centre of it, I found a few fuchsine bodies in one section, but could not find them in any

other sections. Altogether tissues have been examined from fifty to sixty different cases, sometimes four, five, or six sections of the same tissue selected with the determined purpose of subjecting the positive observations to the severest possible tests. The result has been that fuchsine bodies were found in one case of chronic ulcer of the leg, one of tuberculous disease of a joint with old sinuses, one of phenomenally severe destructive and intractable syphilitic lesion. These were cases of which I knew something. Then there were two cases of which I have at present

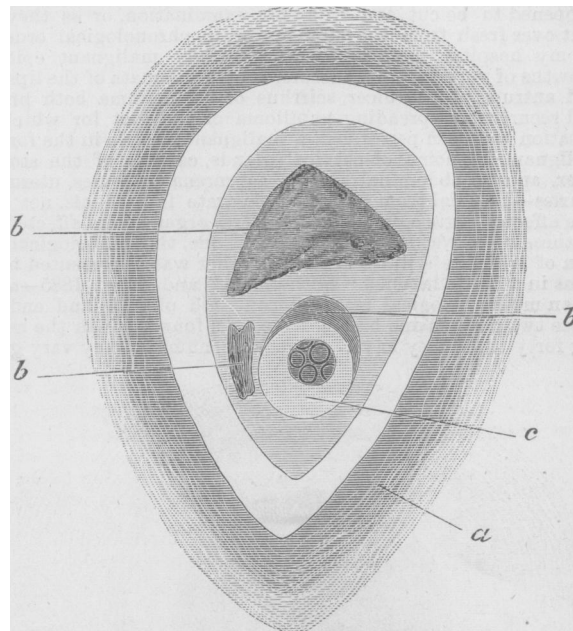


Fig. 7.—Mass of epithelium in alveolus, showing nuclei at *bbb*; *c*, vacuole containing degenerating organism.

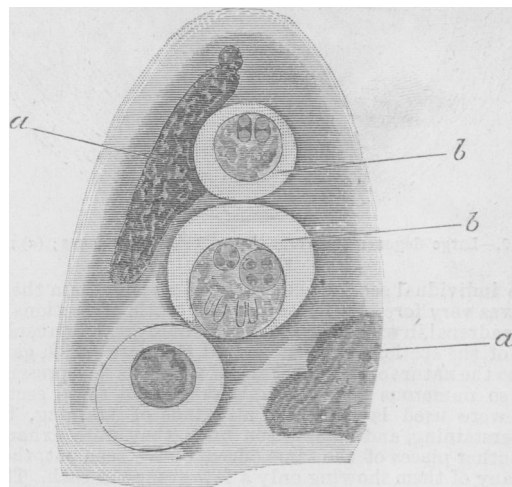


Fig. 8.—Mass of epithelium showing nuclei at *aa*; *bb*, vacuoles containing degenerating organism showing spores.

no record, one a case of mammary adenoma, and one a gummatous tumour of the meninges. I need not dwell upon the possibility of ulcerated free surfaces becoming contaminated by organisms, nor need I do more than remind you that chronic ulcers assume at times malignant characters. With regard to their presence in the remarkable case of syphilis to which I have referred, and also in a gumma of the dura mater, I am at present content to repeat that; in one of these there was a phenomenal destructiveness and intractableness, and in the other probably a like intractableness to treatment, and to indicate the possibility of there having been a dual infection. At all events, I think you will agree with me

that a more severe set of check observations could not have been selected, and the occurrence of the organism in the exceptional cases mentioned could not be regarded as sufficient to overthrow our other evidence. In fact, to my mind, they but suggest possible solutions of various phenomena which have been recognised but hitherto not explained.

So much for the check observations and the negative side, and now I turn to my cases of cancer and the positive side. Forty-five cases have been examined, and that there are not more is simply due to want of time. These were taken either because they happened to be cut and ready for examination, or as they were sent over fresh from the surgeons, or in chronological order out of my hospital material. They include malignant epithelial growths of very varied structure, as epitheliomata of the lips, face, and antrum, rodent ulcer, scirrhus of the mamma both primary and recurrent, a spreading papilloma of the foot for which amputation had been performed, a malignant nodule in the foreskin, malignant adenoma of cervical glands, cancers of the stomach, liver, spleen, abdominal glands, suprarenal capsules, uterus, and ovaries—material from forty-five separate individuals, not forty-five affected organs, for in some several organs were affected. One of these cases was a very remarkable one, the pathological position of which is still uncertain; another was represented by sections in a bottle labelled "epithelioma" and dated 1885—a time when my pathological material consisted of odds and ends. In these two no fuchsine bodies have been found, but in the remaining forty-three they have. As regards number, they vary greatly

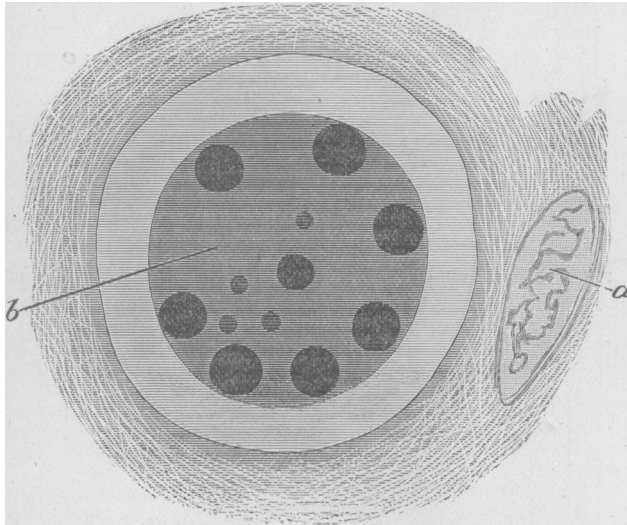


Fig. 9.—Large degenerating organism (b) showing spores; (a) nucleus of epithelium.

in the individual sections cut at the same time from the same bit. This was very forcibly illustrated in a bottle of sections of a cancerous adrenal, in which they were present in great numbers in certain parts of the sections. It was, indeed, this case which gave me the clue to the nature of these organisms, as will be seen presently. They were so numerous and so unmistakable in these sections that they were used lavishly for all kinds of staining, bleaching, counterstaining, and comparison until they were exhausted, and three other pieces of the same adrenal have been cut, the sections from any of them showing only a few groups in each. The special abundance of the bodies in foci was noted in other cases, and may possibly occur in all. I must also say that they are not necessarily present in every section, nor are they necessarily present in every piece of a tumour which may be cut, although we have seldom had to cut two pieces to find them.

As regards their distribution in the various constituents of the morbid growth, they may be present in the small-celled infiltration at the margin of a cancer, as shown in Fig. 1, an early epithelioma of the lip, or amongst and in the epithelial cells in the cancerous alveoli, as in Fig. 2; or in the stroma, or in the lymphatics. In one case of very diffuse infection of mammae, liver, and spleen, etc., I found them in the spleen beyond the malignant nodules. I have also in at least one case seen them in the small-

celled infiltration in a portal space in the liver beyond the cancer nodule.

As a rule, which is comparatively rarely departed from, they occur in little clusters or groups of two, three, four, five, up to twenty or more. Wherever they occur they almost always show a clear space round them. They can be found readily with a lens of 100 diameters if the light is good, and the search is facilitated by the use of an Abbe's substage condenser. Their brilliant red or purplish red colour forms a striking contrast to the green and delicate purple of the tissues, as seen in the coloured figures. The individuals of which the groups consist are in form [perfect

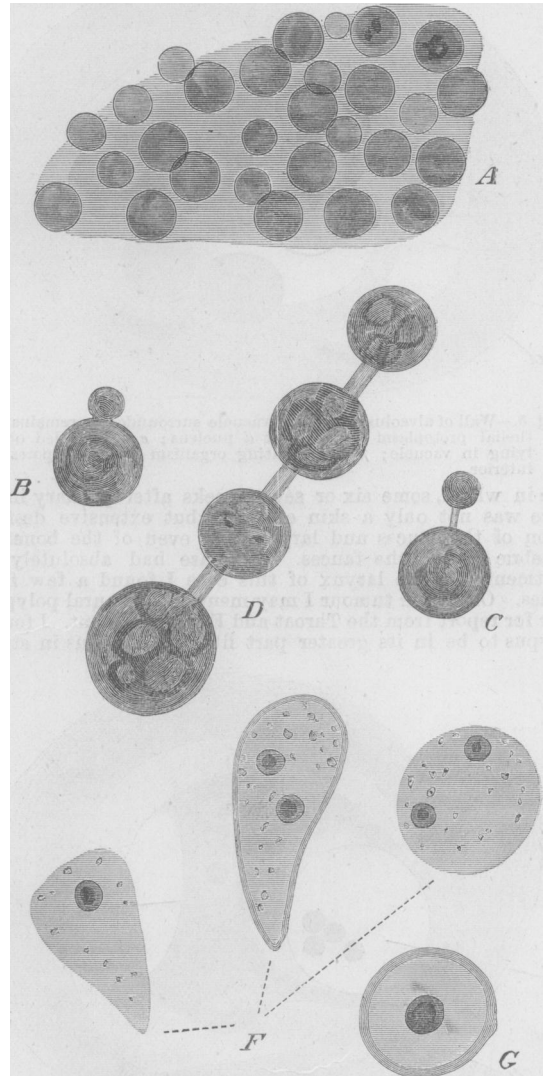


Fig. 10.—A, mass of fungi; B, individual giving off bud; C, same, but bud further removed from parent but still attached; D, four individuals attached to one another; E, four individuals attached and overlapping; F, small spores in lymph cells and leucocyte; G, altered leucocyte containing spore.

spheres. They vary greatly in size, the largest being about 12μ in diameter, that is, half as large again as a red blood corpuscle, others are 11, 10, 9, 8, 4μ , and even much smaller, the commonest size being 4μ . They appear perfectly homogeneous and structureless as examined by daylight, and the larger clumps are held together by a delicate cementing substance which stains faintly. Such are the observations which even an inexperienced microscopist will have no difficulty in making if he has succeeded with the differential staining.

¹ Their internal structure requires artificial illumination for its determination, and it is not dealt with at present.

I must not leave this part of the subject without referring to another complication which troubled me greatly for some time, and that was that the nucleus of the cancer cells retained in some instances the fuchsine dye. This was all the more confusing as the nuclei of the cells in the unaffected tissue did not do so; however, by a process of bleaching the colour could be turned out of the nuclei while the bodies in question still retained it. In the meantime, I cannot more fully dwell on this point, although it includes some exceedingly interesting and important phenomena, which must remain for future consideration.

As it seemed to me, there was no escape from regarding these structures as special organisms which—so far at least as my pathological material was concerned—were practically confined to cancer. The question was, What were they? Were they animal or vegetable? and what was their mode of growth and reproduction? Before attempting to answer this question it is necessary to look at the work which has been done, especially on the Continent, in the study of cancer, and the contentions which have been based upon that work.

The bacilli found in cancer by Scheuerlen,² Verneuil, and Koubasoff may here be passed by, to enable us to reach at once the work which describes a parasite, belonging to the lowest sub-kingdom of animals, as occurring in some cases of cancer. In this connection it is necessary to point out that the first epithelial growth in man in which a parasite of this kind was held to stand in causal connection was, so far as I am aware, molluscum (or epithelioma) contagiosum. Virchow pointed out the resemblance of certain structures in this disease to gregarinæ, but Bollinger³ is entitled to the credit of having more definitely asserted this, owing to the resemblance between this disease as occurring in man, and a similarly named disease in fowls which was specially studied and described by him.

Professor Neisser,⁴ of Breslau, published in 1888 an elaborate paper on this subject containing the results of his own observations, in which he places the parasite in the coccidia group of the sporozoa. The drawings he gives in support of this contention I need not specially refer to, as I am not in a position to form an opinion on them, not having had the opportunity of studying this disease. I may, however, say that I am by no means convinced of his contentions by the figures given.

Last year (1889) two communications were made to the Société de Biologie by Darier, working in Malassez's laboratory, and seemingly inspired by him.⁵ In the first of these,⁶ communicated on March 23rd, he intimated the recognition of a coccidium in a case of *acné cornée*, and defines the condition as a *psorospermose cutanée*; in the second, communicated on April 13th,⁷ he intimated that he had found a parasite belonging to the same class in a case of Paget's disease of the nipple. He says that they present all the degrees or stages of evolution of these organisms; at first a naked mass of protoplasm, afterwards surrounded by a membrane, then dividing into very numerous granules (*orains*) contained in a cyst; and he infers that the disease is a parasitic one, a *psorospermose*. He gives no figures.

To the same Society, on April 6th, 1889,⁸ M. Albarran intimated that he had recognised organisms of a like nature in two epithelial tumours of the jaw. He at the same time mentions that M. Malassez had observed analogous forms in many tumours. He also gives no figures.

In the *Fortschritte der Medicin*⁹ of June 1st, 1889, Professor Thoma has a very short note, without illustrations, on "A Characteristic Parasitic Organism in the Cells of Carcinoma." He describes it as a unicellular organism, consisting of protoplasm and a nucleus, with sometimes a nucleolus. They vary in shape, being round or oval. They are present singly or in groups in the nucleus, the latter becoming vacuolated. In other cases the cyst is near the nucleus. He says there is a strong temptation to regard these as encapsuled coccidia, but this interpretation is still doubtful.

Louis Wickham, on January 1st, 1890, published a long and interesting paper¹⁰ on "The Pathological Anatomy and the Nature

of Paget's Disease of the Nipple," in which he describes and figures appearances which he regards as coccidia or psorospermia.

Professor Klebs published, in June of this year,¹¹ papers "On the Nature and Diagnosis of Cancer Formation," in which he discusses these questions with fairness and masterliness. In them he refers to hyaline bodies present in cancer, which, however, he is decidedly disposed to regard as degenerative products. It is not altogether clear what he means by his hyaline bodies, for he speaks of them as present in the inner parts of the proliferating epithelial tubes, which were filled by them, partly in a rounded, but mostly in an angular form; they were also present in the stroma, but more sparsely. The figure he gives does not help us to form an opinion on the nature of the structures to which he refers. I am, however, disposed to regard most of his hyaline bodies as productions of the cells, for hyaline masses are frequently present, and are easy of recognition in the alveoli of the more adenomatous cancers.

Then, lastly, in July of this year, Von Nils Sjöbring¹² describes a "Parasitic Protozoa-like Organism in Carcinoma," of which he gives figures, and which he found in six cases of cancer of the mamma. He follows it from a simple cellular stage to the stage of spore formation.

Summing this up, and leaving out any further reference to molluscum contagiosum, we find that Albarran, Darier, Thoma, Wickham, and Sjöbring have found in cancer what they believe to be an organism. All of them, with the exception of Thoma, describe their organism as belonging to the protozoa, while Thoma does not commit himself; and, as has been said, only Wickham and Sjöbring give figures to aid us in forming a judgment on their contentions.

With the object of elucidating this subject, I may be permitted to refer briefly to the lowest sub-kingdom of the animal world, which is divided by Leuckart into three classes, the rhizopoda, the sporozoa, and the infusoria. The sporozoa contain, according to Balbiani,¹³ five groups or orders, the gregarinæ, the psorospermia oviformes or coccidia, and three other groups of psorospermia. Of these the gregarinæ occur as parasites in the invertebrates, while the psorospermia occur in the vertebrates. As regards the latter group, it is important to understand their structure and development. They are described by the authorities as unicellular organisms covered by a more or less firm capsule or shell, which latter, in the coccidia, have a double contour and the contents either fill the shell or are gathered into a rounded mass. Reproduction in them all is by means of spores (pseudonavicellæ or psorospermia) formed in the interior of the adult, and in these spores are developed sickle-shaped bodies which escape from the spore and become new parasites.¹⁴ This mode of reproduction is an essential factor in the determination of the biological position of these parasites. To meet this necessity, Sjöbring has figured the spore formation in the cancers he examined.

Wickham's organism consists of a double contoured capsule either filled with protoplasm, or the protoplasm is gathered into a mass in the centre. He does not give any figures of the formation of spores as occurs in typical psorosperms. In fact, looking at the work on this subject in the concrete, I regard some of the figures as having nothing whatever to do with foreign organisms, for I am familiar with the appearances represented; others have certainly been misinterpreted, while some figures probably represent the organism with which I am dealing.

To return now to the consideration of our fuchsine bodies, we have seen that they occur usually in groups, the individuals of which vary greatly in size, but can be seen with the ordinary working lenses magnifying from 300 to 400. For more detailed investigation, I have worked with a No. 7 objective of Leitz and one-sixteenth oil immersion by Reichert, and a No. 3 or No. 5 eyepiece. They may be studied as stained by the special method given here, or by logwood and eosine, or by Gram's method with methyl violet. With reference to logwood, I may say that it does not stain the bodies under consideration, but they are tinted with eosine. Each group, and most of the isolated individuals, is surrounded by a clear area, which clear area has often the appearance of being bounded by a definite capsule. This appearance is brought out in Fig. 2, *et. seq.*, and the study of the isolated fuchsine bodies is necessary for the complete understanding of this interesting

² Die Pathologie des Carcinoms, *Deutsch. med. Woch.*, 1887, p. 48.

³ *Virchow's Arch.*

⁴ *Vierteljahresschrift für Dermatologie und Syphilis*, 1888; Retzius also has a paper which I have not seen: *Om. Mollusc. Contag.*, *Nord. Med. Ark.*, 1870, ii.

⁵ See *Arch. de Méd. Expérimentale et d'Anatomie Pathologique*, March 1st, 1890, p. 302.

⁶ *La Semaine Médicale*, 1889, p. 101.

⁷ *Loc. cit.*, p. 125.

⁸ *Loc. cit.*, p. 117.

⁹ *Fortschritte der Medicin*, No. 11, p. 413, June 1st, 1889.

¹⁰ *Archives de Médecine Expérimentale et d'Anatomie Pathologique*, 1889, p. 46.

¹¹ *Deutsche medicinische Wochenschrift*, Nos. 24, 25, and 32, June, 1890.

¹² *Fortschritte der Medicin*, No. 14, July 15th, 1890.

¹³ *Leçons sur les Sporozoaires*, Paris, 1884; see also *Die Protozoen als Krankheitserreger*, von Dr. L. Pfeffer, Jena, 1890.

¹⁴ Leuckart, *The Parasites of Man*. English Translation.

link in the history of the organism. What I find is this: An isolated individual is present, for example, in an epithelial cell, as in Fig. 3; the cell protoplasm is stained faintly with logwood, and the nucleus is deeply stained, while an eosine-stained globe is present in the cell protoplasm, the globe being surrounded by a clear area or vacuole, which has such a definite limit that it looks somewhat like a capsule, but it can be seen by focussing that the free edge of the naked epithelial cell gives an exactly analogous effect, so that I have no hesitation in saying that there is no true capsule. As regards the clear space itself, while in many places it looks as if it were empty, in others it contains a structureless very transparent substance which tints very delicately. A similar structure is to be found in masses of epithelium (Fig. 7) welded together and lying in spaces. But, both in these epithelial masses and in the vacuoles referred to, there may be small fuchsin bodies surrounded by a clear space and bounded by what we must call either a capsule or a limiting structure. These are represented in Figs. 4 and 5, and their mode of formation has to be dealt with. Now these appearances are of great importance, for on them might be based the contention that here we have to do with an encysted sporozoon, coccidium, or psorosperm. Next, it is to be noted that in the vacuoles there may be two or more small fuchsin bodies (Figs. 3 and 6); in other parts the fuchsin body has become gran-

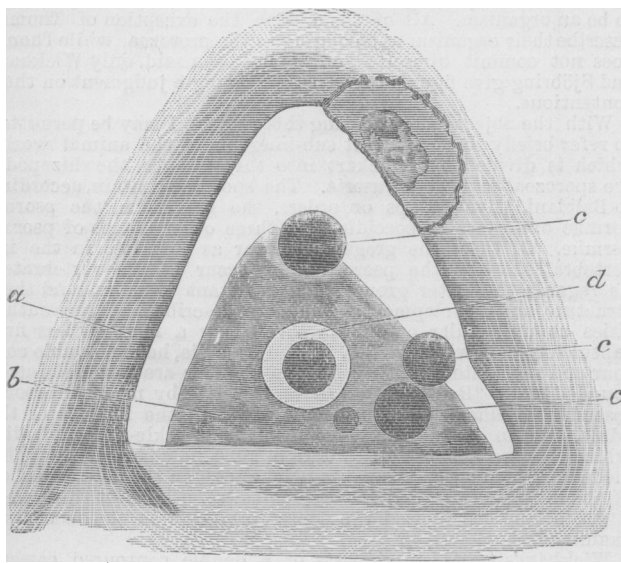


Fig. 11.—Large epithelial cell (b) containing spores (c c c) without vacuole and (d) spore with vacuole.

ular, lost its characteristic staining reaction, but shows in the midst of the granules minute eosine-tinting bodies undoubtedly spores (Figs. 5, 7, 8). Further, I draw attention to Figs. 7 and 8; in them the fuchsin bodies, by our own staining method, are coloured purple instead of red; and this purple colour gave me trouble in my earlier investigations. I then excluded all purple-stained structures, and there is still caution required in the admission of some of them. In these, as the organism becomes granular and degenerates, the spores in it become more visible. In Fig. 9 there is a very large fuchsin body stained purple, and lying in its space and in it spores are very distinctly present. In Fig. 8 there is a large space with four free purple-stained fuchsin bodies, and in the nucleus of an adjoining epithelial cell a similar body which, I take it, has recently migrated; and it is to be noted that this has no vacuole round it. A similar appearance is seen in Fig. 11 (logwood and eosine), where, in a large epithelial cell, there are four fuchsin bodies not surrounded, while one is surrounded by a vacuole.

From all this it might still be contended we were dealing with a protozoon, but I have to draw attention to Fig. 10, from a section stained by Gram's method with methyl-violet. This stain shows the process most diagrammatically, although it is to be observed by other staining methods. Here it is quite unmistakably to be seen that a large fuchsin body gives either off

or out a small globular body (Fig. 10 B), which gradually increases its distance from the parent body, but remains attached to it by a delicate filament (Fig. 10 C); this bud grows and gives off another, and so on, and there is obtained such a figure as is represented in Fig. 10 D. In other cases, however, there are rows, the individuals of which overlap one another, as seen in Fig. 10 A, or a large fuchsin body shows arcs of circles projecting from it. Further, by Gram's method smaller spores can perhaps be seen than by other staining methods, and some appearances are exceedingly suggestive of a parent body having vomited out a number of minute spores. By this same method of staining it can be seen that the small spores appear in the lymphoid cells or leucocytes of the infiltrated area (Fig. 10 F), that the effect of this entrance is that the cell-protoplasm becomes clearer and the chromogenic granules are driven to the circumference of the cell; at all events they disappear, with the result that the small fuchsin body is surrounded by a clear space, with a distinct limiting ring formed by the remains of the comparatively unaltered protoplasm. (Fig. 10 G). This, I take it, is the mode of formation of what we may call the encapsulated fuchsin bodies, lying in vacuoles or amongst epithelial cells, as in Figs. 4 and 5. Now as to the appearances in the interior of the epithelial cells. When the fuchsin body first enters them no vacuole is present (Fig. 11), but a vacuole is produced (Fig. 11 a), this vacuolation being evidently simply a change wrought in the cell protoplasm by the fuchsin body which leads to its clarification, increased transparency, and to a loss of tinting capacity. The limit of this change is a definite line as distinguished from a gradually shaded line, and thus the appearance, which might be mistaken for a capsule, is produced.

From all this there is in my mind absolutely no doubt that the organism here is a fungus which belongs to the sprouting fungi, (*Sprosspilze* of Nägeli.)¹⁵ The proof of this is by no means to be readily found in every section nor in every case, for the usual arrangement—as demonstrable by the fuchsin and iodine green method—is that of clusters. The explanation of this, I think, is that our method of staining acts best when the organism is at a certain stage of its growth, and that the smallest spores and degenerating larger individuals either do not stain differentially or they stain purple from a combination of the two colours used.

In conclusion, it is only necessary for me to remind you that this class of fungi includes the yeast fungus, and that if the presence of this parasitic fungus in cancer is confirmed by other observers, we have found in it an organism which from its very character implies the production of a fermentation product; while the nutrition, the reproduction, and the death of the fungus cannot be conceived as occurring in the tissues without producing changes not disproportionate in magnitude to the anatomical changes present in cancer.

I wish further to take this opportunity of acknowledging the loyal devotion and the untiring industry and zeal, as well as the technical skill and care with which my friend and pathological assistant, Mr. W. F. Robertson, has helped me in this investigation.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

REINFECTION, RECRUDESCENCE, OR WHAT?

THE interest of Dr. Green's case, published in the "Memoranda" for September 27th, is increased by this recurrence of scarlet fever not being in a special hospital for infectious diseases, as in the five others that have come under my notice. Here the patient, as I have been kindly informed, had not mixed with scarlet fever cases in the interval between her first and second attacks, and all risk of reinfection from clothing had been obviated; but she had returned to her room, where she had sickened just three weeks before, and had occupied it for twelve days, up to the second seizure. A relapse or recrudescence is sometimes seen in the second week, when the fading rash again becomes red, and the throat worse; here the second fever is rarely as high as the first, and desquamation is delayed rather than interrupted. In measles,

¹⁵ *Die niederen Pilze*, München, 1877. See also *Fungi, Mycetozoa, and Bacteria*, by A. de Barry, English translation, 1887.